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**COMMENTS**

Please find attached the Appellant's Modified Brief under 37 C.F.R. §41.37 in Response to an Office Action Mailed February 12, 2007, Petition for Extension of Time Under 37 C.F.R. §1.136(a), Power of Attorney and Correspondence Address Indication Form

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | |
|---|---|---|
| Applicant: Lloyd Wolfinbarger, Jr., *et al.* | § | |
| Serial No.: 10/940,545 | § | Group Art Unit.: 3732 |
| Filed: July 23, 2003 | § | Examiner: David C. Cornstock |
| For: PLASTICIZED BONE AND SOFT TISSUE GRAFTS AND METHODS OF MAKING AND USING SAME | § | |

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CERTIFICATE OF FACSIMILE 37 CFR 1.6

I hereby certify that this correspondence is being transmitted to the United States Patent and Trademark Office via facsimile to (571) 273-8300 on April 12, 2007.

Stephanie A. Wardwell
Signature Stephanie A. Wardwell

Sir:

**APPELLANT'S MODIFIED BRIEF UNDER 37 C.F.R. §41.37 IN RESPONSE TO AN OFFICE ACTION MAILED February 12, 2007**

Applicant submits this modified brief in response to the Examiner's objection to the "Summary of the Claimed Subject Matter" section of the Appellant's brief under 37 C.F.R. § 41.37 (C)(1)(v), filed November 8, 2006. In that submission Applicant appealed final rejection and requested an oral hearing. The section objected to has been modified in the current filing.

The Office Action mailed February 12, 2007 set a shortened period for response of March 12, 2007. This paper should be considered as a petition for an Extension of Time sufficient to effect a timely response; please charge any fees or credit any overpayments to Deposit Account No. 50-0310 (067949-5018).

DOCKET NUMBER: 95176562-005004 (64230-00005USD2)
PATENT

## TABLE OF CONTENTS

## I. REAL PARTY IN INTEREST (37 C.F.R. § 41.37 (C)(1)(i))

The real party of interest is Lifenet.

## II. RELATED APPEALS AND INTERFERENCES (37 C.F.R. § 41.37 (C)(1)(ii))

There are no related appeals known to the Appellant.

The application subject to this appeal (the "Wolfinbarger application") is a division of U.S. Patent Application Serial No. 09/107,459, filed June 30, 1998, now U.S. Patent No. 6,293,970, which issued September 25, 2001.

This application was filed in an attempt to provoke an interference with an issued patent, (the "Osteotech patent"), U.S. Patent No. 6,162,258, which issued December 19, 2000, to Nelson L. Scarborough and Todd M. Boyce for "LYOPHILIZED MONOLITHIC BONE IMPLANT AND METHOD FOR TREATING BONE" from U.S. Patent Application Serial No. 09/382,331, filed August 25, 1999. The Osteotech patent did not include a claim to an earlier priority than its filing date.

The Osteotech patent application was filed nearly 14 months after the priority date of the Wolfinbarger application. The only pending claims of the Wolfinbarger application, claims 33 and 34, are identical to claims 1 and 33 of the issued Osteotech patent.

## III. STATUS OF CLAIMS (37 C.F.R. § 41.37 (C)(1)(iii))

Claims 33 and 34, listed in the Claims Appendix, are pending and presently on appeal. Appellant canceled original claims 1-32, without prejudice or disclaimer, August 29, 2001, in a preliminary amendment. In the same amendment, Appellant added claims 33 and 34. These claims have not been amended during the prosecution of the Wolfinbarger application.

This appeal to the Board of Patent Appeals and Interferences is from the final rejection of claims 33 and 34 in the Office Action, mailed March 15, 2005 (hereinafter, "the Final Rejection").

## IV. STATUS OF AMENDMENTS (37 C.F.R. § 41.37 (C)(1)(iv))

No amendments were filed subsequent to the Final Rejection.

## V. SUMMARY OF THE CLAIMED SUBJECT MATTER (37 C.F.R. § 41.37 (C)(1)(v))

The invention relates to a lyophilized monolithic bone implant and a process of treating monolithic bone.

The present invention provides a plasticized bone product that exhibits properties that approximate those properties present in normal hydrated bone (e.g., it is not brittle), that can be readily stored in a lyophilized (e.g., freeze-dried) state, and that does not require rehydration prior to clinical implantation. Appellant's Specification, page 1 lines 4-13, and page 6 lines 16-19.

One aspect of the present invention is directed to methods that include the steps of (1) contacting a monolithic bone (i.e., essentially intact pieces of a femur or tibia, or a whole rib, among others) with at least one biocompatible mechanical strength-conserving agent, (2) subsequently lyophilizing the bone, and (3) packaging the lyophilized bone. A monolithic bone that is contacted with biocompatible mechanical strength-conserving agent as in the present invention is said to be plasticized. Appellant's Specification, page 8 line 20 through page 9 line 9, page 10 lines 10-21, page 19 lines 14-15, page 21 lines 12-16, and Examples 1-10 pp. 22-44.

Biocompatible mechanical strength-conserving agents (plasticizers) of the claimed invention are liquid organic materials that are capable of penetrating and remaining in the bone during its lyophilization, packaging and storage. Appellant's Specification, page 13 lines 1-14, page 14 line 9 through page 15 line 14, and Examples 1-10 pp. 22-44. Examples of types of plasticizers that may be used include: polyols, monoglycerides, and various short- and medium-chain free fatty acids and their corresponding monoacylglycerol esters. Appellant's

Specification, page 14 line 21 through page15 line 5. Specific examples of plasticizers that may be-used include: glycerol (glycerin USP), ethylene glycol, and triethylene glycol, among others. Appellant's Specification, page 15 lines 6-7, page 13 lines 9-10, and Examples 1-10, pp. 22-44.

Another aspect is directed to a monolithic bone that contains at least one biocompatible mechanical strength-conserving agent that has been lyophilized, packaged, and stored. Appellant's specification. page 7 lines 16-17 and Examples 1-10, pp. 22-44.

## VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL (37 C.F.R. § 41.37 (C)(1)(vi))

Claim 33 stands rejected pursuant to 35 U.S.C. §103(a) as being unpatentable over Boyce, *et al.* (U.S. Patent No. 5,899,939) ("Boyce") in view of Morse, *et al.* (U.S. Patent No. 5,333,626) ("Morse").

Claim 34 stands rejected pursuant to 35 U.S.C. §102(e) as being anticipated by Boyce.

## VII. ARGUMENT (37 C.F.R. §41.37 (C)(1)(vii))

The rejections of claim 33 pursuant to 35 U.S.C. §103(a) and claim 34 pursuant to 35 U.S.C. §102(e) are improper and should be reversed. First, the applied prior art references are analyzed. Second, the relevant legal standards are set forth. Third, the errors associated with the rejection of claims 33 and 34 are discussed.

### A. The Prior Art

Boyce discloses a bone-derived implant that is made up of layers of fully mineralized or partially demineralized cortical bone and, optionally, one or more layers of some other material, such as demineralized bone, graphite, or pyrolytic carbon. Because the layers constituting the implant are assembled into a unitary structure, an implant exhibiting good overall load-supporting properties is provided.

Morse discloses a method for treating bone and making it suitable for transplantation. The method includes contacting bone with a global decontaminating agent, cleaning the bone, and terminally decontaminating the cleaned bone. The invention also provides a method of cleaning bone, which can include contacting the bone with detergent under high pressure washing conditions at elevated temperatures.

### B. The Law Regarding Anticipation and Obviousness

The Federal Circuit has held that anticipation under 35 U.S.C. § 102 requires that each and every element of the claimed invention be disclosed in a single prior art reference. *See, e.g., In re Spada*, 911 F.2d 705, 708, 15 U.S.P.Q.2d (BNA) 1655, 1657 (Fed. Cir. 1990); *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 U.S.P.Q.2d (BNA) 1913, 1920 (Fed. Cir. 1989).

For anticipation, "[t]here must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q.2d (BNA) 1001, 1010, *clarified on reconsideration*, 18 U.S.P.Q.2d (BNA) 1896 (Fed. Cir. 1991).

Additionally, to be patentable an invention must be nonobvious over the prior art as set forth in 35 U.S.C. § 103:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The determination of obviousness and, thus, patentability, is based on several underlying factual determinations: "(1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) the extent of any proffered objective indicia of nonobviousness, sometimes termed secondary considerations." *Rockwell Int'l Corp. v. United States*, 147 F.3d 1358, 1362, 47 U.S.P.Q.2d 1027, 1029 (Fed. Cir. 1998); *accord Graham v. John Deere Co.*, 383 U.S. 1, 17, 148 U.S.P.Q. 459 (1966).

In addition to disclosing the claimed subject matter, the prior art must be enabled as it must be able to "teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation." *3M v. Chemque, Inc.*, 303 F.3d 1294, 1306, 64 U.S.P.Q.2d (BNA) 1270, 1278 (Fed. Cir. 2002).

C. Analysis

The rejection of the pending claims is erroneous for the reasons discussed below. Boyce does not teach the claimed invention recited in claims 33 and 34, even if taken in combination with Morse. Moreover, while Boyce is likely enabling for its own claims it is not enabling for the invention the Examiner has conceived using the roadmap of Wolfinbarger's claims. Given proper consideration, the conclusion that Appellant's claims are unpatentable should be withdrawn.

The Examiner's rejection of claims 33 and 34 comprises three sentences. One is conclusory and the other two are in error. With respect to claim 33, the Examiner concludes:

> Boyce et al. disclose the claimed invention except for explicitly disclosing packaging of the implant.

Final Rejection at 3. The remaining portion of the rejection of claim 33 relates to Morse's disclosure of packaging. The entirety of the Examiner's rejection of claim 34 states the following:

> Boyce et al. disclose a monolithic bone implant, *i.e.* whole bone or a portion of a whole bone, 20 that is contacted with a liquid organic agent, *i.e.* a type of polyethylene glycol, and freeze-dried, *i.e.* lyophilized (see col. 1, lines 6-17; col. 2, lines 9-15; col. 4, lines 20-24 and 45-46; col. 4, line 53-65; col. 5, lines 21-29; and col. 6, lines 8-13, 45-46 and 51-52. It is noted that providing layers and dimeralizing the implant are both optional; therefore, the scope of the disclosure includes mineralized bone that is not provided with the layers (id.).

Final Rejection at 2.

The statement regarding claim 34 is inaccurate on at least two counts. First, Boyce does not teach a bone implant where "providing layers ...[is] optional," or a "mineralized bone that is not provided with the layers." Final Rejection at 2. Boyce teaches two or more layers of bone. *See* col. 1, lines 11-14 ("[T]his invention relates to a bone-derived implant which is made up of

two or more layers at least one of which is fully mineralized or partially demineralized cortical bone and, optionally, one or more layers fabricated from some other material."); col. 3, lines 12-16 ("The bone-derived implant of the present invention comprises at least two superimposed layers at least one of the layers being a compression strength-imparting layer derived from nondemineralized cortical bone or cortical bone which has been only partially demineralized."); col. 2, lines 27-30 ("Depending on the thickness of the layers, there can be anywhere from 2 to about 200 layers overall in the bone-derived implant."); col. 4, line 1-15 ("Assembling the superimposed layers into a strong unitary structure ..."); col. 4, lines 20-24 ("In addition to its compression strength-imparting fully mineralized or partially mineralized cortical bone layers, the bone-derived implant of this invention can optionally possess one or more layers formed from one or more other materials."); col. 4, lines 34-44 ("If desired, the compression strength axis of one or more compression strength-imparting layers can be offset relative to the compression strength axis of one or more of the other compression strength-imparting layers in an arrangement much like that of plywood."); Example 1 (layers); Example 2 (layers); Example 3 (layers) (emphasis added throughout). Layers are not "optional"; layers are Boyce's invention.

However, assuming for the sake of argument that Boyce teaches that the provision of layers is optional, Boyce does not teach a bone "that is contacted with a liquid organic agent, *i.e.* a type of polyethylene glycol, and freeze-dried, *i.e.* lyophilized." Final Rejection at 2. Such a teaching cannot be found anywhere in Boyce. The Examiner points to Example 1. There no discussion whatsoever in Example 1 regarding "contacting the bone with a mechanical strength-conserving amount of at least one biocompatible mechanical strength-conserving agent, said agent being a liquid organic material which is capable of penetrating and remaining in the bone during its lyophilization, packaging and storage" prior to lyophilition as required by claim 33 nor

is there a teaching of a "lyophilized monolithic bone implant containing at least one biocompatible mechanical strength-conserving agent, said agent being a liquid organic material which is capable of penetrating and remaining in the bone during its lyophilization" as required by claim 34. Such claimed features are not disclosed.

Moreover, the idea of a "freeze-dried" product is not discussed anywhere else in Boyce. Not in the object of the invention, not in the detailed description, not in the claims. Examples 2 and 3 do not mention it. How can Boyce be said to anticipate claim 34 or disclose the claimed invention of claim 33 (except for explicitly disclosing packaging of the implant)?

In the Response to Arguments section the Examiner continues to make unsupported conclusory statements. Here, he asserts that "In example 1, still referring to 'this invention,' Boyce continues to disclose that the bone, which has already been shown to explicitly include a liquid organic agent such as a polyethylene glycol, can be freeze-dried (see col. 6, lines 45-46 and 50-52)." *See* Final Rejection at 4. As stated above, Example 1 lacks any disclosure whatsoever of any liquid organic agent. Example 1 (col. 6, lines 46-57) is reproduced below:

> EXAMPLE 1
>
> A cortical section of bone from the diaphyseal region was cut in the longitudinal direction while continuously wetted with water into approximately 1.5 mm thick layers using a diamond-bladed saw. The layers were then frozen to -70°C. and freeze-dried for 48 hours. The layers were then assembled with cyanoacrylate adhesive and held in a clamp for two hours while the adhesive set. The resulting multilayered unitary structure was cut on a band saw and shaped by grinding and machining with a hand-held motorized shaping tool to provide a shaped bone implant.

There is no disclosure of a liquid organic material before or after the "layers" were freeze-dried. Additionally, the Examiner is slightly overstating Boyce's teachings to state that Boyce "explicitly include[s] a liquid organic agent such as polyethylene glycol" when what Boyce

actually states is: "fatty acid esters such as laureate, myristate and stearate monoesters of polyethylene glycol". Col. 5 lines 21-23. This is not an "explicit" teaching of "polyethylene glycol."

Moreover, the teaching of Example 1 is to contact bone with water and then freeze-dry it. Water is not a liquid organic material. Water is not a "biocompatible mechanical strength-conserving agent, said agent being a liquid organic material" as required by claims 33 and 34.

The Examiner asserts in the Response to Arguments section that "Boyce does explicitly say that the various substances, including the liquid organic material, 'can be incoporated into the bone-derived implant of *this invention* or any of its constituent layers during *any* stage of the assembly of the implant,' which necessarily includes the stage wherein the bone is freeze-dried (col. 5, lines 24-28)." Final Rejection at 5 (emphasis in Final Rejection). As stated above, there is no disclosure of such an incorporation in Example 1 and for the reasons that follow Boyce is not enabling for such a teaching.

First, the various substances discussed in column 5 require one or more channels, *see* col. 4, line 53 to col. 5, line 32, which are not provided in Examples 1 or 2 or Figure 2. Channels are only provided in relation to Example 3 and Figures 5 and 6. *See* col. 6, lines 26-36 ("Because of the open structure of implant 50 resulting from the pattern of longitudinal channels 52 and transverse channels 53, the implant permits the vascular penetration or host bone ingrowth therein and/or the diffusion of one or more medically/surgical useful substances therefrom.") (emphasis added); col. 7, lines 1-8.

Second, the laundry list of "various substances" (col. 4 line 53 to col. 5 line 32) does not teach subsequent lyophilization of bone treated with fatty acid esters, or any other substances that promote bone growth and healing. In fact, among the substances listed as possible growth

enhancers, along with the fatty acid esters, are living cells and blood. At least these components of the list would generally not be suitable for lyophilization, because lyophilization can be detrimental to their growth promoting and healing properties.

Moreover, the dehydrated layers produced in Example 1 are assembled with a cyanoacrylate adhesive. It is known that acid compounds hinder or prevent the polymerization of cyanoacrylate esters making cyanoacrylate adhesive ineffective. Substances other than acids can also interfere with the ability of a cyanoacrylate adhesive to bond to surfaces together. Thus, surfaces of the layers of bone fixed to each other with cyanoacrylate adhesive, as in Example 1, would need to be non-acidic to permit the adhesive to work. At least some of the substances for promoting or accelerating bone growth contemplated by Boyce can be acidic (*i.e.*, amino acids, among others). Other substances contemplated by Boyce (*i.e.*, cartilage fragments) can also interfere with securely bonding two bone surfaces together using a cyanoacrylate adhesive. There is no teaching in Boyce contemplating the compatibility of adhesives with specific substances introduced into a bone layer prior to its being fixed to another layer. One cannot infer, based on Example 1, that lyophilization is contemplated for anything other than natural cortical bone.

Therefore, Boyce and Morse taken alone or together do not teach every element of the claimed invention as recited in claims 33 and 34 and are not enabling for the purposes of the Examiner's interpretation.

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PATENT

For the foregoing reasons, the rejection of claims 33 and 34 should be withdrawn and the application forwarded to the Issue branch.

Respectfully submitted,

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## VIII. CLAIMS APPENDIX (37 C.F.R. §41.37 (C)(1)(viii))

33. A method for treating monolithic bone intended for implantation to conserve the mechanical strength of the bone during lyophilization and subsequent packaging and maintain such strength during the storage of the bone, the method comprising:

a) contacting the bone with a mechanical strength-conserving amount of at least one biocompatible mechanical strength-conserving agent, said agent being a liquid organic material which is capable of penetrating and remaining in the bone during its lyophilization, packaging and storage;

b) lyophilizing the bone containing the mechanical strength-conserving agent; and,

c) packaging the lyophilized bone.

34. A lyophilized monolithic bone implant containing at least one biocompatible mechanical strength-conserving agent, said agent being a liquid organic material which is capable of penetrating and remaining in the bone during its lyophilization, packaging and storage.

## IX. EVIDENCE APPENDIX (37 C.F.R. §41.37 (C)(1)(ix))

No evidence was submitted pursuant to 37 C.F.R. §§ 1.130, 1.131, or 1.132 into the record during the prosecution of the Wolfinbarger application.

## X. RELATED PROCEEDINGS APPENDIX (37 C.F.R. §41.37 (C)(1)(x))

There are no related proceedings known to the Appellant. However, should the present appeal be granted, an interference proceeding with regard to the Osteotech patent is requested.